

Efficacy of The Ginger on Chemotherapy-Induced Nausea and Vomiting (CINV): A Systematic Review

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Keywords: Zingiber officinale, ginger, CINV, nausea, vomiting, emesis, chemotherapy

Abstract: Background: Chemotherapy Induced Nausea-Vomiting (CINV) is a frequent side effect experienced by sufferers of malignant tumor undergoing chemotherapy. Ginger is one herb that has been used since many years and is naturally especially as antiemetic. This study aims to find out the effectiveness of ginger against nausea vomiting due to chemotherapy by systematic review and followed the PRISMA statement guidelines. Methods: Scopus, Science Direct, PubMed, and Springerlink database from January 2012 – December 2017. Articles identified by using search terms or keywords ('CINV' OR 'nausea' OR 'vomiting' OR 'emesis') AND ('chemotherapy') AND ('ginger' OR 'Zingiber officinale' OR 'rhizoma'). All included studies were access base on randomized controlled trial. Results: 14 out of 209 papers were including. Articles that have been reviewed results that ginger give benefits to reduce nausea vomiting due to chemotherapy showed a significant especially in acute phase. Conclusions: Nausea vomiting is a side effect of the chemotherapy modalities can be treated by ginger and used as evidence to justify of complementary therapies.

1 INTRODUCTION

Chemotherapy Induced Nausea-Vomiting (CINV) is a term used to describe the incidence of nausea, vomiting and a combination of both of the symptoms associated with the granting of cytotoxic chemotherapy (Marx *et al.*, 2016). CINV is a frequent side effect experienced by sufferers of malignant undergoing chemotherapy (Mizuno *et al.*, 2016). 70-80% of patients receiving chemotherapy experiencing CINV (Chase *et al.*, 2018). Nausea and vomiting are common symptoms that can weaken and cause a decrease in quality of life, dehydration, electrolyte imbalances, weight loss and delay the granting of chemotherapy (Davidson *et al.*, 2012; Kittelson, Elie and Pennypacker, 2015). Therefore nurses play an important role in the treatment of patients with CINV (Middleton and Lennan, 2011).

Pharmacological therapy in the form of 5-HT₃ receptor antagonists and NK₁ receptor antagonists have been widely used and is the first choice for treatment and prevention of CINV (Ranganath, Einhorn and Albany, 2015). Despite having been given antiemetic, 44.6% of patients experiencing nausea and/or vomiting during the 120 hours after given chemotherapy (Escobar *et al.*, 2015). Herbal

therapy is one complementary therapy can be used as a supporting therapy for cancer patients undergoing chemotherapy. One of the plants and herbs that can be used are Ginger (*Zingiber officinale*) (Panahi *et al.*, 2012).

Ginger is one herb that has been used since many years and is naturally especially as antiemetic (Lete and Allué, 2016). Some research suggests that ginger effective at reducing nausea vomiting, motion sickness, seasickness, post surgery, as well as pregnancy (Lee and Shin, 2016; Koçak, Yücepur and Gökler, 2017; Kusumawardani *et al.*, 2018).

This study aims to find out the effectiveness of ginger on nausea vomiting due to chemotherapy.

2 METHODS

This systematic review followed the Preferred Reporting Item for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Liberati *et al.*, 2009).

Search strategy

Scopus, PubMed, ScienceDirect and Springerlink databases were searched for articles published from

January 2011 – December 2017. The search terms used were; ('CINV' OR 'nausea' OR 'vomiting' OR 'emesis') AND ('chemotherapy') AND ('ginger' OR '*Zingiber officinale*' OR 'rhizoma').

Eligibility Criteria

Types of studies

Random controlled trial and/or crossover studies

Types of participants

The main inclusion criteria entailed adult (18 years or older), patients receiving chemotherapy of any emetogenicity level.

Type of interventions

Ginger is used as the main and specific interventions to assess effectiveness against nausea and vomiting.

Type of outcomes measures

Primary outcomes is to assess the frequency and severity of nausea vomiting due to chemotherapy.

Study selection

The protocol standard for selecting research studies is suggested in the PRISMA method for systematic review followed by screening by removing duplicates, then three reviewers selecting titles, abstracts, and keywords, then deleting irrelevant quotes according to the selection criteria. Reviewers noted the reasons for choosing such research studies including selection of inclusion data. Selection of research studies that have been recorded by three reviewers and then compared to one another to be adjusted feasibility with the criteria set. Secondly, to minimize the risk of incorrect study entry in selection there are several research studies that have been applicable or can be applied in a review by one or two reviewers to be included in the next review stage. Full text of the articles is obtained if the title and abstract meet the inclusion criteria or if the feasibility study is clearly resolved by a joint discussion between the reviewers.

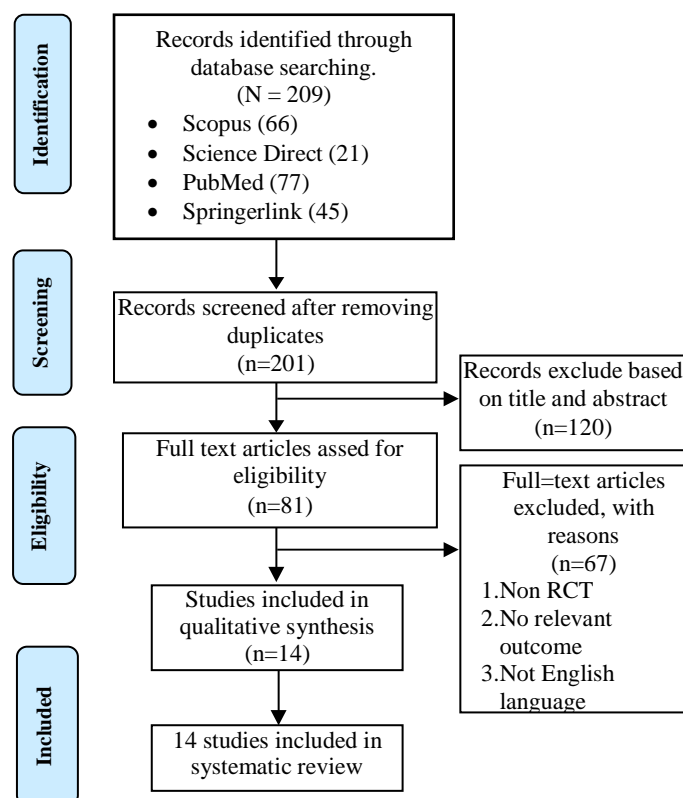


Figure 1: Flow Diagram

3 RESULTS

Literature search and study selection

A total of 14 studies were identified for inclusion in the review. The search of Scopus, PubMed, Science Direct and Springerlink databases provided a total of 209 citations. After adjusting for duplicates 201 remained. Of these, 120 studies were discarded because after reviewing the abstract it appeared that these papers clearly did not meet the criteria. The full text of the remaining 81 citations was examined in more detail. It appeared that 67 studies did not meet the inclusion criteria as described. See flow diagram Figure 1.

Study Characteristic

Methods

All 14 studies finally selected for review were randomized controlled trials published in English.

Table 1: Characteristic of included studies

No.	Study	Methods	Participants	Interventions	Control	Outcomes	Results
1	Anti-Emetic Effect of Ginger Powder Versus Placebo as an Add-On Therapy in Children and Young Adults Receiving High Emetogenic Chemotherapy (Pillai <i>et al.</i> , 2011).	Prospective, double-blind, randomized single.	Respondents were patients aged 8 - 21 years with bone cancer diagnoses who received chemotherapy with levels potential high emetogenic. The number of patients 60, divided into two groups (interaction and control), each of which amounted to 30 respondents.	Provision of ginger capsules. The dose of administration is determined by weight. The dose consist of 20 - 40 kg: 167 mg per capsule and 40 - 60 kg: 400 mg per capsule. All respondents received antiemetic therapy such as Ondansetron and Dexamethasone according to standard (4-8 mg).	Provision of starch powder capsule (placebo). The dose of administration is determined by weight. The weight 20- 40 kg: 167 mg per capsule and 40 - 60 kg: 400 mg per capsule.	Grades of nausea and vomiting as measured by Edmonton's Symptom Assessment Scale (ESAS) and National Cancer Institute (NCI) guidelines.	Ginger capsules effectively at reducing acute nausea in moderate severity ($p = 0.003$), acute vomiting ($p = 0.002$) and delayed nausea ($p = 0.001$), delayed vomiting ($p = 0.022$).
2	Effect of Ginger on Chemotherapy Induced Nausea and / or Vomiting in Cancer Patients (Alparslan <i>et al.</i> , 2012).	Randomized controlled trial.	Respondents were cancer patients who received chemotherapy at a hematology clinic numbering 45 and divided into 2 groups, Intervention group: 15 and control group: 30.	Ginger tablet 800 mg/day. Tablets are given in the morning and evening (@ 400 mg). Before being given ginger, respondents were given antiemetic protocol (Setron 3 mg through intravenous).	Antiemetic drugs according to protocol (Setron 3 mg via intravenous).	Nausea and/or Vomiting follow-up form.	Ginger is effective for reducing nausea and vomiting due to chemotherapy ($p < 0.05$).
3	Effect of Ginger on Acute and Delayed Chemotherapy - Induced Nausea and Vomiting: A Pilot, Randomized, Open-Label Clinical Trial (Panahi <i>et al.</i> , 2012).	Randomized, open-label, clinical trial.	Respondents were cancer patients in unit of Baqiyatallah Hospital Oncology which amounted to 100 respondents and divided into two groups, each of which amounted to 50 respondents.	Giving of ginger capsule 3 x 500 mg for 4 days and antiemetic regimen according to protocol (Granisetron and Dexamethasone).	Antiemetic regimens according to protocol (Granisetron and Dexamethasone).	Prevalence and severity of CINV. (Rhodes Index of Nausea, Vomiting, and Retching / RINVR).	Ginger may decrease the prevalence of nausea 6 - 24 h post chemotherapy but cannot reduce the prevalence and severity of acute or delayed phase vomiting.

No.	Study	Methods	Participants	Interventions	Control	Outcomes	Results
4	Ginger (Zingiber officinale) reduces acute chemotherapy-induced nausea: a URCC CCOP study of 576 patients (Ryan <i>et al.</i> , 2012).	Randomized controlled trial.	Respondents were cancer patients aged ≥ 18 years and had undergone 1 cycles of chemotherapy amounting to 576 respondents. Respondents were divided into 4 groups: a. The intervention group I (n: 134). b. Group of interventions II (n: 141). c. The intervention group III (n: 152). d. Control group (n: 149).	Giving for 6 days (2 times a day), starting at 3 days prior to chemotherapy. The dosage of ginger is divided into 3 types according to the group. Each respondent received antiemetic drugs according to the protocol (Antiemetic 5-HT 3 and Dexamethasone). Group of intervention I: ginger capsule 0,5 gr. Group of intervention II: ginger capsule 1.0 gr. Infection group III: ginger capsule 1.5 gr.	Provision of antiemetic drugs according to protocol (Antiemetic 5-HT 3 and Dexamethasone).	Average Nausea severity (NAv) and Maximum Nausea severity (NMx).	Giving of 0.5 gr - 1.0 gr significantly at reducing the severity of nausea due to chemotherapy in cancer patients ($p = 0.017$).
5	Effect of Herbal Therapy to Intensity Chemotherapy-Induced Nausea and Vomiting in Cancer Patients (Montazeri <i>et al.</i> , 2013).	Randomized cross-over clinical trial.	Respondents were cancer patients who had undergone at least 2 cycles of chemotherapy, a total of 44 respondents and divided into two groups (intervention and control), each of which amounted to 22 respondents.	Giving 4 x 250 mg ginger capsule . 2 capsules given 30 minutes before receiving chemotherapy drugs, 2 capsules given 6 hours after chemotherapy. Each respondent received antiemetic according to protocol 30 minutes before chemotherapy, i.e. 3 mg Grainestrone (Keitrile) and 8 mg Dexamethasone.	Antiemetic drugs according to protocol and placebo in the form of 250 mg of ineffective powder capsule (Chickpea powder).	Intensity of vomiting and the way of investigation, by Kortila Tools.	Ginger is more effective at reducing the frequency and intensity of nausea of vomiting due to chemotherapy than placebo.

No.	Study	Methods	Participants	Interventions	Control	Outcomes	Results
6	Can ginger ameliorate chemotherapy-induced nausea? Protocol of a randomized double-blind, placebo-controlled trial (Marx <i>et al.</i> , 2014).	Double-blinded randomized-controlled trial.	Respondents were chemotherapy patients who had a history of emetogenic > 18 years old of 146 respondents and divided into two groups (intervention and control), each with 73 respondents.	Provision of 300 mg ginger capsules. Each capsule contains 5% gingerol, 15 mg active ingredient in gelatin capsule. Capsules are given 4 x 300 mg for 5 days starting on the first day of chemotherapy. Each patient is given antiemetic medication; 5HT 3 (Ondansetron) Antagonists, Corticosteroids (Dexamethasone), and NK1 receptor antagonists (Aprepitant).	The placebo capsule contains 300 mg of inactive/reacting material.	Rhodes Inventory of Nausea, Vomiting and Retching (INVR).	Ginger effective at reducing nausea vomiting due to chemotherapy.
7	Oral intake of ginger for chemotherapy-induced nausea and vomiting among women with breast cancer (Arslan and Ozdemir, 2015).	Randomized, controlled trial.	60 respondents who underwent outpatient at Oncology hospital in Turkey. Respondents were divided into two groups (intervention and control) of 30 respondents respectively.	Provision of ginger powder twice daily for 3 days. Ginger is given as much as 500 mg mixed into 1 tablespoon of yogurt. Each respondent received standard antiemetic drugs according to the protocol. 5-HT 3 receptor antagonists Palonosetron (Aloxi®), Dexamethasone (Decadron®), Antihistamine, And Ranitidine (Zantac®) administered by intravenous, and Aprepitant (Emend ®) administered orally.	Provision of standard antiemetic drugs.	Nausea severity was evaluated using a numeric scale with a severity.	The severity of nausea and the number of episodes of vomiting were lower in the intervention group than the control group ($p < 0.05$), but did not affect the retching period ($p > 0.05$).

No.	Study	Methods	Participants	Interventions	Control	Outcomes	Results
8	Effects of inhaled ginger aromatherapy on chemotherapy-induced nausea and vomiting and health-related quality of life of women with breast cancer (Lua, Salihah and Mazlan, 2015).	Single-blind, controlled, randomized cross-over study.	Respondents were cancer patients at the Sultanah Nur Zahirah (HSNZ) hospital and hospital King Zainab II, Malaysia, which is numbered 75 respondents. Respondents were divided into two groups. Intervention group (n: 38) and Control group (n: 37).	Giving ginger aromatherapy neck for 5 days (day and night). The necklace is 20 cm from the nose. Every 3 times a day, the aromatherapy necklace is brought under the nose and the respondent is asked to inhale deeply with duration 2 minutes for 3 periods. The aromatherapy necklace contains two drops of ginger essential oil.	Giving aroma-therapy necklace containing two drops of perfume ginger.	VAS nausea score, frequency of vomiting. Quality of life: HRQoL profile (EORTCQLQ-C30 scores).	Nausea score was significantly lower in the intervention group (ginger essential oil) than placebo during the acute phase ($p = 0.040$). There was no significant effect on the frequency of vomiting.
9	Efficacy of Ginger in Control of Chemotherapy Induced Nausea and Vomiting in Breast Cancer Patients Receiving Doxorubicin-Based Chemotherapy (Ansari <i>et al.</i> , 2015).	Randomized controlled trial.	Respondents were breast patients who received Doxorubicin chemotherapy as many as 150 respondents. Respondents were divided into two groups (intervention and control), each of which amounted to 75 respondents.	Giving 2 x 250 mg ginger capsule for 3 days. All respondents were given premedication therapy that is Dexamethasone 16 mg intravenous (IV), Aprepitant 125 mg orally and Granisetron 3 mg IV. Dexamethasone 8 mg oral and oral 80 mg Aprepitant continued for up to two days.	The placebo capsule contains 250 mg of starch powder.	Nausea and vomiting severity (Numeric Scale).	There was no significant difference between intervention and control groups, but in the intervention group there was a decrease in nausea score after the second day of chemotherapy and decreased severity of vomiting.

No.	Study	Methods	Participants	Interventions	Control	Outcomes	Results
10	Effect of Ginger and Chamomile on Nausea and Vomiting Caused by Chemotherapy in Iranian Women with Breast Cancer (Sanaati <i>et al.</i> , 2016).	Randomized, double-blind and clinical trial study.	Respondents are women with breast cancer amounted to 45 respondents. Respondents are divided into three groups, each numbering 15 respondents.	There are two intervention groups. Group A gets 2 x ginger capsule 500 mg. Intervention begins 5 days before up to 5 after chemotherapy. Group B gets the capsule Matricaria chamomilla 2 x 500 mg. Interventions begin to be given 5 days before up to 5 after chemotherapy. All respondents received the regimen Antiemetics of Dexamethasone, Metoclopramide and Aprepitant.	Group C (control) only received antiemetic regimens (Dexamethasone, Metoclopramide and Aprepitant).	Nausea and vomiting severity (Visual Analogue Scale/VAS).	Ginger and chamomile can reducing the frequency of vomiting. No difference which is significantly associated with vomiting between groups of ginger and Chamomile. Ginger is more significant at reducing the frequency of nausea than chamomile.
11	Efficacy of ginger for prophylaxis of chemotherapy-induced nausea and vomiting in breast cancer patients receiving Adriamycin-cyclophosphamide regimens: a randomized, double-blind, placebo-controlled, crossover study (Thamlikitkul, Srimuninnimit and Akewanlop, 2016).	Randomized, double-blind, placebo-controlled, crossover study.	Respondents were 34 and divided into 2 groups. The intervention group: (n = 19) and control group: (n = 15). Population obtained from Oncology clinic at Home Pain Siriraj. Respondents devoted to women ≥ 18 years with a diagnosis of breast cancer.	Ginger capsules 500 mg twice day for 5 days starting from day first in the chemotherapy cycle second. The first dose is given 30 minutes before chemotherapy. Ginger capsules are obtained from Government Pharmaceutical Organization in Thailand. Each capsule ginger contains 500 mg of dried ginger.	Placebo.	Nausea and vomiting severity (Visual Analogue Scale / VAS).	There is no significant difference among respondents given intervention ginger capsules and placebo on the occurrence of vomiting with certain severity, medication use, adherence chemotherapy, and effects side (p = 0,3).

No.	Study	Methods	Participants	Interventions	Control	Outcomes	Results
12	A randomized, double-blind, placebo-controlled, multicenter study of a ginger extract in the management of chemotherapy-induced nausea and vomiting (CINV) in patients receiving high dose cisplatin (Bossi <i>et al.</i> , 2017).	Randomized, double-blind, placebo-controlled, multicenter study.	Respondents numbered 244. Divided into 2 groups of treatment. Intervention group (n = 121) and control group (n = 123)	Gingular capsule ginger 40 mg. At the first and second intervention each patient is given 2 boxes. Each box consists of 8 blisters which correspond to 120 gelatin gel capsules containing vegetable oil (110 mg) and 40 mg ginger extract. Instructions for patients are consuming 2 capsules in the morning and 2 capsules at night with 150 ml of water.	Placebo.	Nausea and vomiting severity (visual analogue scale) and Functional Living Index Emesis (FLIE) questionnaires.	There was no significant difference in the effects of ginger in reducing the effects of nausea due to cisplatin as long as two cycles of chemotherapy, with no benefit in delay, anti-interfering and intercycle assessment, but there was a decrease in nausea score in female patients (p = 0.048) and in patients with Head Neck Cancer (p = 0.038).
13	A phase II randomized double-blind placebo-controlled study of 6-gingerol as an anti-emetic in solid tumor patients receiving moderately to highly emetogenic chemotherapy (Konmun <i>et al.</i> , 2017).	Multicenter randomized, double-blind, placebo-controlled.	Respondents were patients with a histologic diagnosis of solid tumors and aged ≥ 18 years. Respondents numbered 96 divided into two groups. Intervention group (n = 46) Control group (n = 48).	Provision of ginger capsules containing 5 mg 6-gingerol 6-jaheol (1.4% ginger extract). Ginger capsules are given starting 3 days before chemotherapy up to 1 day after chemotherapy.	Placebo capsule containing diluent/binder (microcrystalline cellulose PH 102; Avicel PH 102) and Thixotropic thickening (colloidal silicon dioxide) to suit the weight of 6-gingerol capsules.	Numerical Rating Scale (NRS) using Edmonton's Symptom Assessment Scale (ESAS) The quality of life will be measured by the Functional Assessment of Cancer Therapy-General (FACT-G) instrument.	6 - Gingerol significantly increases overall CR level at CINV, appetite and quality of life of cancer patients undergoing to adjuvant stage III chemotherapy (p <0.001).

No.	Study	Methods	Participants	Interventions	Control	Outcomes	Results
14	The Effect of a Standardized Ginger Extract on Chemotherapy - Induced Nausea-Related Quality of Life in Patients Undergoing Moderately or Highly Emetogenic Chemotherapy: A Double Blind, Randomized, Placebo Controlled Trial (Marx <i>et al.</i> , 2017).	Double-blind, randomized placebo-controlled trial.	Respondents with 51 numbers were divided into two groups. The intervention group (n = 24) and the control group (n = 27).	Group I: Allocated to intervention. Participants followed three cycles of chemotherapy to evaluate the effect of intervention during the chemotherapy treatment period. For each cycle, the results were assessed 3 days before chemotherapy until 4 days post chemotherapy (i.e., for 7 days). Participants were asked to take capsules 4 times per day each meal, for 5 days per chemotherapy cycle. The capsules contain 300 mg of standard ginger extract an 15 mg of the ingredients active.	Placebo.	Functional Living Index Emesis 5 Day Recall (FLIE-5DR) and the Rhodes Inventory of Nausea, Vomiting and Retching (INVR).	Ginger is effective for reducing nausea and vomiting due to chemotherapy. There is no significant result in Cycle 2. In Cycle 3, global QoL (p = 0.040) and fatigue (p = 0.013) were significantly better in the intervention group compared with placebo.

Population

The included studies involved 1.801 participant. The main inclusion criteria entailed adult (18 years or older), receive a chemotherapy of any emetogenicity level (Marx *et al.*, 2014). Most of the participants were on combination chemotherapy regimens with moderately or highly-emetogenic, such as cisplatin and doxorubicin, docetaxel, epirubicin, cyclophosphamide, fluorouracil (Pillai *et al.*, 2011; Panahi *et al.*, 2012; Ansari *et al.*, 2015; Konmun *et al.*, 2017; Marx *et al.*, 2017). (Alparslan *et al.*, 2012; Ryan *et al.*, 2012; Arslan and Ozdemir, 2015; Lua, Salihah and Mazlan, 2015; Sanaati *et al.*, 2016; Thamlikitkul, Srimuninnimit and Akewanlop, 2016; Bossi *et al.*, 2017; Hayes *et al.*, 2017) lacked information regarding the chemotherapy agents and regimens.

Interventions

The form of the ginger treatment was encapsulated ginger, which contained ginger root powder (167 mg or 400 mg) (Pillai *et al.*, 2011), powdered and dried ginger root (300 mg or 500 mg) (Panahi *et al.*, 2012; Montazeri *et al.*, 2013; Marx *et al.*, 2014, 2017; Ansari *et al.*, 2015; Sanaati *et al.*, 2016; Thamlikitkul, Srimuninnimit and Akewanlop, 2016; Bossi *et al.*, 2017), The 6-gingerol capsules contained a ginger extract, referenced as 6-gingerol 5 mg (1.4% w/w of ginger extract) (Konmun *et al.*, 2017). Alparslan *et al.*, (2012) receive ginger tablets (800 mg). Purified liquid extract of ginger root (0.25 g) containing gingerols, zingerone, and shogaol (Ryan *et al.*, 2012). Participants received 500 mg powdered ginger, mixed with a spoonful of yogurt to make swallowing easier (Arslan and Ozdemir, 2015). Patients received 5-day aromatherapy treatment using either ginger essential oil (Lua, Salihah and Mazlan, 2015). All participant received standard nausea and vomiting-preventing medications (5-HT₃ antagonist receptor and dexamethasone).

Outcomes

Nausea and vomiting frequency was evaluated using rating scale such as visual analog scales (Lua, Salihah and Mazlan, 2015; Sanaati *et al.*, 2016; Thamlikitkul, Srimuninnimit and Akewanlop, 2016; Bossi *et al.*, 2017), assigning scores to strain tool of intensity of vomiting (Montazeri *et al.*, 2013). Ryan *et al.*, (2012); Arslan and Ozdemir, (2015); Ansari *et al.*, (2015) were using numeric scale for severity of nausea and vomiting. Panahi *et al.*, (2012); Marx *et al.*, (2014, 2017) were using form of the Rhodes

Inventory of Nausea, Vomiting and Retching (INVR). Grade of nausea and vomiting as measured by Edmonton's Symptom Assessment Scale (ESAS) (Pillai *et al.*, 2011; Konmun *et al.*, 2017).

Results of individual studies

The data of 3 of 14 articles in the review stated that there were no significant effects of the grant of the ginger against nausea vomiting of chemotherapy (Ansari *et al.*, 2015; Thamlikitkul, Srimuninnimit and Akewanlop, 2016; Bossi *et al.*, 2017).

Ginger can reduce the severity of nausea and vomiting in the acute phase (Pillai *et al.*, 2011; Arslan and Ozdemir, 2015) and reduce the frequency and intensity of nausea vomiting in the acute phase (Alparslan *et al.*, 2012; Panahi *et al.*, 2012; Ryan *et al.*, 2012; Montazeri *et al.*, 2013; Marx *et al.*, 2014; Arslan and Ozdemir, 2015; Lua, Salihah and Mazlan, 2015; Sanaati *et al.*, 2016; Konmun *et al.*, 2017). The two articles stated that ginger can also reduce the frequency and severity of nausea vomiting on a delayed phase (Pillai *et al.*, 2011; Marx *et al.*, 2017).

The majority of the studies mentioned ginger effectively and safely used to decrease nausea vomiting due to chemotherapy. (Arslan and Ozdemir, 2015; Konmun *et al.*, 2017) reported no side effects arising from the use of ginger.

4 DISCUSSION

Some research has examined the effect of ginger on control CINV gives different results, but the vast majority of researchers stated that ginger can decrease the frequency, intensity and severity of nausea and vomiting due to chemotherapy. Thamlikitkul, Srimuninnimit and Akewanlop, (2016); Bossi *et al.*, (2017) states that there is no significant difference between the groups given ginger and placebo at reducing nausea vomiting of chemotherapy. There are several things that can affect the results of the research-related effectiveness of ginger against nausea vomiting include characteristics of respondents, the regimen of chemotherapy, the use of antiemetic, preparation of capsules of ginger, ginger dose is given, and the length of the grant Ginger.

There are differences of opinion related to the influence of the ginger against CINV on acute phase or delay (delay). Ansari *et al.*, (2015) mention ginger more effectively decreases the nausea vomiting on a phase delay. Pillai *et al.*, (2011); Panahi *et al.*, (2012); Ryan *et al.*, (2012); Arslan and

Ozdemir, (2015); Lua, Salihah and Mazlan, (2015) stated that ginger effective at reducing nausea vomiting due to chemotherapy in acute phase.

The side effects of chemotherapy in the form of nausea vomiting can lead to heavy stress to the patient. Stimulates enterochromaffin cells chemotherapy agents in the digestive tract to release serotonin receptor triggers with serotonin. Receptor activation triggers a vagal afferent pathways active activates the vomiting Center and cause response throw up. The potential of the Emetic chemotherapy agent itself is the main stimulus against the nausea and vomiting caused by chemotherapy (Chemotherapy Induced Nausea and Vomiting/CINV).

5 CONCLUSIONS

This review explains that systematic intervention ginger potentially as effective therapy for nausea and vomiting. The urgency of use ginger as a therapy requires more investigation, but safe and can be tolerated well by the participants as a therapeutic modality nonfarmakologis.

Ginger is one of the effective herbal remedies to treat nausea and vomiting did not result in any side effects. Antiemetic activity on ginger obtained caused by elements of the gingerols and shogaols, both phenolic compounds. The content of 5-Hydroxytryptamine₃ receptor antagonist on ginger who is also one of the cornerstone therapy antiemetic such as granisetron and ondansentron.

REFERENCES

- Alparslan, G. B. *et al.* (2012) 'Effect of Ginger on Chemotherapy-Induced Nausea and / or Vomiting in Cancer Patients', (January 2017).
- Ansari, M. *et al.* (2015) 'Efficacy of ginger (G) in control of chemotherapy induced nausea and vomiting (CINV) in breast cancer patients (BCPs) receiving doxorubicin-based chemotherapy (DBCT)', *Annals of Oncology*, 26, p. ix115. doi: 10.14456/apjcp.2016.186/APJCP.2016.17.8.3877h <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4131259/>.
- Arslan, M. and Ozdemir, L. (2015) 'Oral intake of ginger for chemotherapy-induced nausea and vomiting among women with breast cancer.', *Clinical journal of oncology nursing*, 19(5), pp. E92-7. doi: 10.1188/15.CJON.E92-E97.
- Bossi, P. *et al.* (2017) 'A randomized , double-blind , placebo-controlled , multicenter study of a ginger extract in the management of chemotherapy-induced nausea and vomiting (CINV) in patients receiving high dose cisplatin'.
- Chase, D. M. *et al.* (2018) *Palliative Care and Quality of Life*. Ninth Edit, In *Clinical Gynecologic Oncology*. Ninth Edit. Edited by P. J. DiSaia *et al.* Elsevier Inc. doi: 10.1016/B978-0-323-40067-1.00020-6.
- Davidson, W. *et al.* (2012) 'Malnutrition and Chemotherapy-Induced Nausea and Vomiting: Implications for Practice', *Oncology Nursing Forum*, 39(4), pp. E340-E345. doi: 10.1188/12.ONF.E340-E345.
- Escobar, Y. *et al.* (2015) 'Incidence of chemotherapy-induced nausea and vomiting with moderately emetogenic chemotherapy: ADVICE (Actual Data of Vomiting Incidence by Chemotherapy Evaluation) study', *Supportive Care in Cancer*, 23(9), pp. 2833-2840. doi: 10.1007/s00520-015-2809-3.
- Hayes, P. D. *et al.* (2017) 'Topical oxygen therapy promotes the healing of chronic diabetic foot ulcers: a pilot study', *Journal of Wound Care*, 26(11), pp. 652-660. doi: 10.12968/jowc.2017.26.11.652.
- Kittelson, S. M., Elie, M.-C. and Pennypacker, L. (2015) 'Palliative Care Symptom Management', *Critical Care Nursing Clinics of North America*. Elsevier Inc, 27(3), pp. 315-339. doi: 10.1016/j.cnc.2015.05.010.
- Koçak, İ., Yücepur, C. and Gökler, O. (2017) 'Is Ginger Effective in Reducing Post-tonsillectomy Morbidity? A Prospective Randomised Clinical Trial', *Clinical and Experimental Otorhinolaryngology*, 11(1), pp. 65-70. doi: 10.21053/ceo.2017.00374.
- Konmun, J. *et al.* (2017) 'A phase II randomized double-blind placebo-controlled study of 6-gingerol as an anti-emetic in solid tumor patients receiving moderately to highly emetogenic chemotherapy', *Medical Oncology*. Springer US, 34(4). doi: 10.1007/s12032-017-0931-4.
- Kusumawardani, P. A. *et al.* (2018) 'Effect of Ginger Drinks on Nausea Vomiting in the First Trimester of Pregnancy', *IOP Conference Series: Materials Science and Engineering*, 288(1). doi: 10.1088/1757-899X/288/1/012161.
- Lee, Y. R. and Shin, H. S. (2016) 'Effectiveness of Ginger Essential Oil on Postoperative', X(X), pp. 1-5. doi: 10.1089/acm.2015.0328.
- Lete, I. and Allué, J. (2016) 'The effectiveness of ginger in the prevention of nausea and vomiting during pregnancy and chemotherapy', *Integrative Medicine Insights*, 11, pp. 11-17. doi: 10.4137/IMLS36273.
- Liberati, A. *et al.* (2009) 'The PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of Studies That Evaluate Health Care Interventions : Explanation and Elaboration', 6(7). doi: 10.1371/journal.pmed.1000100.

- Lua, P., Salihah, N. and Mazlan, N. (2015) 'Effects of inhaled ginger aromatherapy on chemotherapy-induced nausea and vomiting and health-related quality of life in women with breast cancer', *Complementary Therapies in Medicine*. Elsevier Ltd. doi: 10.1016/j.ctim.2015.03.009.
- Marx, W. *et al.* (2014) 'Can ginger ameliorate chemotherapy-induced nausea? Protocol of a randomized double blind , placebo-controlled trial', pp. 1–11.
- Marx, W. *et al.* (2016) 'Chemotherapy-Induced Nausea and Vomiting: A Narrative Review to Inform Dietetics Practice', *Journal of the Academy of Nutrition and Dietetics*. Elsevier Inc, 116(5), pp. 819–827. doi: 10.1016/j.jand.2015.10.020.
- Marx, W. *et al.* (2017) 'The Effect of a Standardized Ginger Extract on Life in Patients Undergoing Moderately or Highly'. doi: 10.3390/nu9080867.
- Middleton, J. and Lennan, E. (2011) 'induced nausea and vomiting', 20(17).
- Mizuno, M. *et al.* (2016) 'Gynecologic Oncology A prospective observational study on chemotherapy-induced nausea and vomiting (CINV) in patients with gynecologic cancer by the CINV Study Group of Japan', *Gynecologic Oncology*. Elsevier Inc., 140(3), pp. 559–564. doi: 10.1016/j.ygyno.2015.12.029.
- Montazeri, A. S. *et al.* (2013) 'Effect of Herbal Therapy to Intensity Chemotherapy-Induced Nausea and Vomiting in Cancer Patients', *Iranian Red Crescent Medical Journal*, 15(2), pp. 101–6. doi: 10.5812/ircmj.4392.
- Panahi, Y. *et al.* (2012) 'Effect of Ginger on Acute and Delayed Chemotherapy-Induced Nausea and Vomiting', *Integrative Cancer Therapies*, 11(3), pp. 204–211. doi: 10.1177/1534735411433201.
- Pillai, A. K. *et al.* (2011) 'Anti-Emetic Effect of Ginger Powder Versus Placebo as an Add-On Therapy in Children and Young Adults Receiving High Emetogenic Chemotherapy', (September 2010), pp. 234–238. doi: 10.1002/pbc.
- Ranganath, P., Einhorn, L. and Albany, C. (2015) 'Management of Chemotherapy Induced Nausea and Vomiting in Patients on Multiday Cisplatin Based Combination Chemotherapy', *BioMed Research International*, 2015. doi: 10.1155/2015/943618.
- Ryan, J. L. *et al.* (2012) 'Ginger (Zingiber officinale) reduces acute chemotherapy-induced nausea: a URCC CCOP study of 576 patients', pp. 1479–1489. doi: 10.1007/s00520-011-1236-3.
- Sanaati, F. *et al.* (2016) 'Effect of ginger and chamomile on nausea and vomiting caused by chemotherapy in Iranian women with breast cancer', *Asian Pacific Journal of Cancer Prevention*, 17(8), pp. 4127–4131. doi: 10.7314/APJCP.2016.17.8.4127.
- Thamlikitkul, L., Srimuninnimit, V. and Akewanlop, C. (2016) 'Efficacy of ginger for prophylaxis of chemotherapy-induced nausea and vomiting in breast cancer patients receiving adriamycin – cyclophosphamide regimen: a randomized , double-blind , placebo-controlled , crossover study', *Supportive Care in Cancer*. Supportive Care in Cancer. doi: 10.1007/s00520-016-3423-8.